0.9% sodium chloride solution was used (using pH as criterium). The study was planned and executed before the 2009 ADA (American Diabetes Association) criteria for resolution of DKA was changed to include the anion gap.[2,3] Therefore, our first aim was to examine if time to resolution based on pH was indeed prolonged with 0.9% saline.

We agree that the pH is not the best marker for resolution of DKA and that the anion gap or even better direct estimation of beta-hydroxybuterate should be preferred.[4,5] On hindsight, we also agree that the study would have been improved if we also included these measurements and evaluated the possible discrepancy between the various definitions of resolution. We did a limited number of beta-hydroxybuterate measurements in this study to determine its association with pH and bicarbonate. However, not all patients had measurements done till resolution so we were not able to compare resolution between pH and ketone criteria.

Of greater interest also would be the practical implications of such misclassification if it exists (extra IV fluid used, possible relapse, time to discharge, etc.).

With regard to Van der Heijden's[6] concerns about coexisting alkalosis, none of the patients in the study had severe vomiting or severe sepsis (other that pneumonia), which could have resulted in alkalosis masking the metabolic acidosis. The most common precipitant for the DKA was patient failure to take prescribed insulin. Patients with severe sepsis who needed inotropic support or mechanical ventilation were also excluded from the study (as stated).

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Advance Access Publication 12 February 2012

Profound hyponatraemia following a tramadol overdose

Sir,

Hyponatraemia is a common electrolyte disturbance associated with prolonged hospitalization and increased mortality. Among numerous aetiologies, tramadol is not routinely included in the list of causative medications. This case highlights an important biochemical side effect, and symptoms that may be easily overlooked without appropriate investigation.

A 56-year-old man presented to hospital 12 h after an intentional overdose of 60 tramadol (50 mg) tablets and 20 co-dydramol (10/500) tablets. The past medical history included COPD, treated with spiriva and seretide inhalers. There was no other current or previous medication use.

On examination, he was drowsy with pinpoint pupils and a respiratory rate of six breaths per minute. Blood pressure was 135/80 mmHg and heart rate 110 beats per minute. Initial arterial blood gases confirmed type 2 respiratory failure (pH 7.25, pCO_2 9.63, pO_2 6.56 on air). Chest radiography showed no significant abnormality. There was rapid improvement with boluses of intravenous nalaxone and an infusion was commenced.

Blood biochemistry sent on admission showed a serum Na 136^+ mmol/l, K^+ 4.2 mmol/l and creatinine 106 umol/l. Liver function tests, paracetamol and salicylate levels were within normal ranges. He was rehydrated with 3 l of intravenous normal saline.

The following day psychiatry input was requested and repeat serum electrolytes indicated a

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Na^+ of 132 mmol/l, K^+ 4.6 mmol/l and creatinine of 57 umol/l.

On the third day, the patient became agitated. Serum electrolytes now measured Na^+ 119 mmol/l, K^+ 4.8 mmol/l and creatinine 40 umol/l; and was confirmed on a repeat sample. The patient was clinically euvolaemic and otherwise remained well with no evidence of infection. Further tests showed normal blood glucose, random cortisol (552 mmol/l) and thyroid function (TSH 1.85 mu/l, FT4 14.20 pmol/l). Serum osmolality was reduced at 242 mmol/l and calculated at 251. Both urinary osmolality and urinary Na^+ were elevated at 208 mmol/l and 36 mmol/l, respectively.

The patient was commenced on a 1 l/day fluid restriction for a diagnosis of SIADH, and unfortunately self-discharged from hospital. Community psychiatry follow-up was arranged.

The syndrome of inappropriate anti-diuretic hormone release (SIADH) represents a diagnosis of exclusion for euvolaemic hyponatraemia, particularly among hospital patients with CNS disorders including head trauma, neoplastic disease, acute and chronic pulmonary disorders and a plethora of iatrogenic drug-related aetiologies. The biochemical disturbances arise from inappropriate water retention at the level of the collecting duct resulting in dilutional hyponatraemia. Serum osmolality is genuinely low (<280 mmol/l) with a normal osmolar gap and not attributable to hyperglycaemia, thyroid disease or adrenal suppression. Urine osmolality is inappropriately elevated (>100 mmol/l) indicating the process of ongoing water retention. Urinary sodium is high (>30 mmol/l) indicating the absence of sodium conservation that occurs with hyponatraemia due to diarrhoea, nephrotic syndrome, cardiac or liver failure.[1]

Tramadol is a centrally acting synthetic opioid analgesic and 3 g was ingested by our patient alongside 10 g of paracetamol and 200 mg of dihydrocodeine. Opioids are known to affect renal excretion of water and sodium, through numerous mechanisms that result in anti-diuresis.[2] In addition, tramadol enhances release of serotonin to achieve its full analgesic effect, and selective serotonin reuptake inhibitors (e.g. venlafaxine) are known culprits in hyponatraemia by stimulating ADH release.[3,4] Therefore, both opioid and serotonin pathways may have acted in synergy to result in profound symptomatic hyponatraemia following a life-threatening overdose.

An awareness of this severe metabolic and neurological disturbance, currently not listed in the British National Formulary,[5] is especially important in the context of a patient already obtunded by the ingestion of opiates.

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